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Editorial

aEEG and cEEG: Two complementary techniques to assess seizures and encephalopathy in neonates

Editorial on "Amplitude-integrated EEG for detection of neonatal seizures: A systematic review" by Rakshasbhuvankar et al.☆

Electrographic seizures are frequent in critically-ill neonates [1]. In one of the most common conditions in the neonatal intensive care unit – hypoxic-ischemic encephalopathy – seizures occur in approximately 30–60% of patients [2,3]. Most electrographic seizures occur in high-risk populations such as patients with hypoxic-ischemic encephalopathy, stroke, cardiac surgery, extracorporeal membrane oxygenation, or meningitis, but can also occur in other neurologic and systemic conditions. Many neonatal seizures present with only subtle or no clinical signs [2]. Only the recent widespread use of continuous electroencephalogram (cEEG) monitoring has revealed the burden of electrographic seizures in critically-ill patients. cEEG monitoring is growing exponentially at an approximate pace of 30% per year in both adults and children. Further, this increase in cEEG use is likely to continue: in a survey of 137 intensivists and neurophysiologists from 97 ICUs in the USA showed that, in an ideal situation with unlimited resources, respondents would monitor 10–30% more patients (depending on the specific indication for cEEG) and 18% of respondents would increase cEEG duration [3]. Electrographic seizure detection in the intensive care unit is a relatively new and developing field in constant evolution.

The rationale for detecting electrographic seizures rests on the assumption that detection and treatment will ultimately lead to improvement. It is currently unknown whether electrographic seizures independently damage the brain or whether they are mere biomarkers of a worse underlying brain injury that is not going to improve with antiepileptic drug treatment. A growing body of literature demonstrates that electrographic seizure burden is independently associated with worse outcomes and suggests that electrographic seizures independently contribute to brain damage. If we assume that electrographic seizures are damaging the brain and antiepileptic drugs stop seizures and improve outcomes, then we would not like to miss electrographic seizures. A recent cost-effectiveness study showed that cEEG monitorization for 24–48 h is relatively inexpensive as it yields goods electrographic seizure detection rates for a moderate price [4]. The American Clinical Neurophysiology Society's guidelines on cEEG in neonates state that "conventional video-EEG monitoring is the gold standard for neonatal seizure detection and quantification and should be used whenever available for seizure detection and differential diagnosis of abnormal appearing, paroxysmal clinical events" [5]. However, cEEG monitorization is resource intensive and requires costly equipment, and demanding schedules from technologists and EEG readers. Both the cost-effectiveness analysis and the American Clinical Neurophysiology Society's guideline are based on current monitoring practices where cEEGs are placed on patients with a high clinical suspicion of seizures.

If cEEG monitoring spreads to lower-risk neonates, costs may skyrocket. Therefore, screening strategies that identify patients at higher risk for seizures are needed. Amplitude-integrated EEG (aEEG) uses a limited montage – typically 2–4 electrodes – and compresses the EEG tracing in time to provide a global overview of brain cerebral activity. aEEG is a cheaper and much less resource-intense alternative to cEEG. With relatively simple training, intensivists and nurses can recognize the most frequent EEG patterns and detect seizures in real time. On the other hand, as a "reduced" version of cEEG, aEEG only provides a rough overview of brain activity and may miss seizures that occur far from the electrodes. In this issue of Seizure, Rakshasbhuvankar et al. provide a systematic review on the diagnostic efficacy of aEEG compared with the current gold standard of cEEG.

This study shows that aEEG yields highly variable sensitivities and specificities and therefore the authors conclude that aEEG cannot be recommended as the mainstay for diagnosis and management of neonatal seizures. This conclusion is perfectly valid based on the current data, and several points may be worth highlighting.

aEEG performance partially depends on the degree of expertise and familiarity with aEEG reading: studies on neonatologists or other aEEG reading-trained personnel yielded sensitivities and specificities in the 80–100% range, but performance dropped dramatically in other groups. Further, not all aEEG set-ups are equal; different technical factors such as number and location of

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electrodes, filter settings, computerized algorithms, and display outputs may influence performance. Future studies may have to take into account the aEEG set-up and the reader's expertise as potential confounders. It may also be helpful to test different aEEG set-ups in the same reader both before and after a training intervention.

aEEG may be even superior to cEEG in some aspects such as simplicity and timeliness. Intensive care unit personnel typically require an electrophysiologist interpreting cEEGs, but, if properly trained, neonatal intensive care unit personnel can directly interpret aEEG at the bedside. Not needing an intermediate EEG reader to extract the information from the aEEG output empowers the intensive care unit personnel to real-time identification of seizures and major changes in brain activity. In contrast, cEEG does not usually provide a real monitorization because data are interpreted only intermittently and rarely in real time. Seizures may be missed due to the very limited montage. In that sense, aEEG may be compared to heart auscultation – a method that can be easily applied at the bedside in real time by any provider – while cEEG may be compared to echocardiography – a specialized method that can only be used intermittently as it requires an additional doctor to interpret the results, and both evaluations are valuable and complement each other.

The study by Rakshasbhuvankar et al. evaluates seizure detection as it is an easily quantifiable outcome, but the value of aEEG does not reside only in detecting seizures. aEEG provides other less quantifiable outcomes. The evaluation of the EEG background and its changes over time is also clinically helpful. The aEEG output permits identification of changes in global trends in brain activity over time better than the detailed output of cEEG.

In summary, the study by Rakshasbhuvankar et al. is a timely summary of a relevant topic: the place of aEEG in electrographic seizure detection in neonates. The presented data suggest that aEEG is a very good screening tool that identifies neonates who need a cEEG: those with EEG backgrounds associated with a high risk for seizures and those with seizures detected on aEEG. In this context, it is important to remember that even the gold-standard – cEEG for 24–48 h – is also just a screening tool as it may miss seizures that occur prior to cEEG placement and after cEEG discontinuation. While the gold standard remains cEEG, it may not be feasible in every neonate around the world immediately. In our current practice, we currently use both techniques complementarily, with immediate set up of the aEEG at the bedside, and replacement with cEEG by a skilled technician, usually rather within minutes than hours and as soon as practically feasible. Future cost-effectiveness and outcome studies on the yield of cEEG and aEEG may help delineate further which option is best for individual neonates treated in different settings and presenting with different risk factors for electrographic seizures.

Conflict of interest

Iván Sánchez Fernández is funded by a grant for the study of Epileptic Encephalopathies from "Fundacion Alfonso Martín Escudero" and the HHV6 Foundation. Tobias Loddenkemper serves on the Laboratory Accreditation Board for Long Term (Epilepsy and Intensive Care Unit) Monitoring, on the Council (and as Treasurer) of the American Clinical Neurophysiology Society, on the American Board of Clinical Neurophysiology, as an Associate Editor for Seizure, as Contributing Editor for Epilepsy Currents, and as an Associate Editor for Wyllie's Treatment of Epilepsy 6th edition. He is part of pending patent applications to detect and predict seizures and to diagnose epilepsy. He receives research support from the Epilepsy Research Foundation, the American Epilepsy Society, the Epilepsy Foundation of America, the Epilepsy Therapy Project, PCORI, the Pediatric Epilepsy Research Foundation, Cure, HHV-6 Foundation, and received research grants from Lundbeck, Eisai, Upsher-Smith, Acorda, and Pfizer. He serves as a Scientific Advisor for Upsher Smith and Lundbeck. He performs video electroencephalogram long-term and ICU monitoring, electroencephalograms, and other electrophysiological studies at Boston Children's Hospital and affiliated hospitals and bills for these procedures and he evaluates pediatric neurology patients and bills for clinical care. He has received speaker honorariums from national societies including the AAN, AES and ACNS, and for grand rounds at various academic centers. His wife, Dr. Karen Stannard, is a pediatric neurologist and she performs video electroencephalogram long-term and ICU monitoring, electroencephalograms, and other electrophysiological studies and bills for these procedures and she evaluates pediatric neurology patients and bills for clinical care.

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